April 18, 2002

James A. Deyo, D.V.M., Ph.D., D.A.B.T.
Technical Associate
Eastman Chemical Company
P. O. Box 431
Kingsport, Tennessee 37662

Dear Dr. Deyo:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2-heptanone, posted on the ChemRTK HPV Challenge Program Web site on December 3, 2001. I commend Eastman Chemical Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Eastman Chemical Company advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
2 - Heptanone (Methyl N–Amyl Ketone)

SUMMARY OF EPA COMMENTS

The sponsor, Eastman Chemical Company, submitted a test plan and robust summaries to EPA for methyl n-amyl ketone (CAS# 110-43-0; 2-heptanone) dated October 4, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on December 3, 2001.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical and Environmental Fate Data. All appropriate SIDS-level tests/estimations have been performed. However, the submitter needs to provide additional data in its biodegradation robust summary.

2. Health Effects. All appropriate SIDS-level tests have been performed. However, the submitter needs to address several deficiencies in the robust summaries.

3. Ecological Effects. The submitted ecotoxicity data are adequate and no further testing is required. Additional information needs to be provided in the acute fish toxicity robust summary.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE 2 - HEPTANONE (METHYL N-AMYL KETONE) CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The submitter's approach to these endpoints is acceptable for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The submitter's approach to these endpoints is acceptable for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate test data are available for these endpoints although the submitter needs to address a few deficiencies in the robust summaries (see "Specific Comments on Robust Summaries").

Acute Toxicity. Acute oral and inhalation toxicity tests in rats are adequate. The acute oral toxicity test in mice appears inadequate. The submitter needs to address the deficiencies noted in the robust summaries. No additional acute toxicity tests are needed.

Repeated Dose Toxicity. Both 10-month inhalation toxicity study in rats and monkeys and a 13-week oral gavage study in rats are adequate.

Genetic Toxicity (in vitro). Studies on reverse mutation in *Salmonella typhimurium* and on chromosomal aberration in Chinese hamster ovary cells adequately address genetic toxicity endpoints.

Reproductive/Developmental Toxicity. A combined reproductive/developmental inhalation toxicity study in rats is adequate for these endpoints although certain information is missing in the robust summary.

Ecotoxicity (fish, invertebrate, and algae). Adequate test data are available for acute fish, daphnia, and algae toxicity. Additional details are needed in the robust summary for the acute fish toxicity test.

Specific Comments on the Robust Summaries

Environmental Fate.

Biodegradation. The submitter needs to provide information on the source/concentration of the microbial inoculum, initial concentration of the chemical, and time required for 10 % biodegradation to take place.

Fugacity. To estimate transport and distribution, the sponsor used the EPIWIN Level III model which provides estimated values as default inputs. EPA recommends using the EQC level III model from the Canadian Environmental Modeling Centre at Trent University, which allows full control of data inputs. This model can be found at the following Web address: http://www.trentu.ca/academic/aminss/envmodel/.

Health Effects.

Acute oral toxicity. For both studies, the submitter needs to add, if available, all dose levels, and the number of animals at each dose. The submitter needs to clarify the LD_{50} for the acute oral toxicity test in mice because the result of the study stated no deaths noted at any dose.

Acute inhalation toxicity. The submitter needs to add the method by which the test atmosphere was generated (e.g., as aerosol, vapor, etc.).

Repeated-dose inhalation toxicity. The submitter needs to clarify the three exposure groups, to add the method by which the test atmosphere was generated (e.g., as aerosol, vapor, etc.), and to specify the hematological, clinical chemistry, and urinalysis parameters assessed.

Repeated-dose oral toxicity. The submitter needs to add the frequency of data collection (for clinical signs, body weight, and food and water intake), the specific hematology, clinical chemistry and urinalysis parameters that were examined, and the specific organs that were weighed or examined for gross and microscopic pathology.

Reproductive/Developmental Toxicity (inhalation). Although the study is considered adequate, information missing from the robust summary includes: the method for generating the test atmosphere, the timing of exposure days in both sexes in relation to mating and gestation, the timing of final sacrifices with respect to gestation and lactation, and the maternal and paternal endpoints that were analyzed (including the specific organs weighed and examined histologically).

Ecotoxicity. The following information is missing from the acute fish robust summary: the test substance purity, number of fish tested, and concentrations tested.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.